

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/B2004/003481

International filing date (day/month/year)
08.10.2004

Priority date (day/month/year)
09.10.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/00, A61K9/10, A61K9/12, A61K31/165, A61K31/56

Applicant
JAGOTEC AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

10/574334
IAP20 REG PCT/PTG 31 MAR 2006
International application No.
PCT/IB2004/003481

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/003481

Box No. II Priority

1. ☐ The following document has not been furnished:

- ☐ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
4. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-19,24,25,28
	No: Claims	20-23,26,27
Inventive step (IS)	Yes: Claims	
	No: Claims	1-28
Industrial applicability (IA)	Yes: Claims	1-28
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

PCT/IB2004/003481

The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

- D1: WO 03/074024 A1 (CHIESI FARMACEUTICI S.P.A; DAVIES, REBECCA, JAINE; GANDERTON, DAVID; L) 12 September 2003 (2003-09-12)
- D2: US 2002/018753 A1 (BLONDINO FRANK E ET AL) 14 February 2002 (2002-02-14)
- D3: US-A-6 054 488 (OLIVER ET AL) 25 April 2000 (2000-04-25)
- D4: WO 00/48587 A1 (NOVARTIS AG; NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H; CLARK) 24 August 2000 (2000-08-24)
- D5: US-B1-6 475 467 (KELLER MANFRED ET AL) 5 November 2002 (2002-11-05)

The documents considered in the present processing are consecutively numbered D1-D5; this numbering results from the citations D1-D5 found in the Search Report (SR) of the corresponding PCT application. It will be adhered to in the rest of the procedure. The cited passage(s) for each citation will be considered unless otherwise specified.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty

1. The technical features of claims 20-23,26,27 are disclosed by documents D1 and D2 and therefore do not fulfill the requirements of Art 33 (2) PCT.
2. Regarding claim 26: A product is only defined by its components and not by its intended use. "Instructions" for using a product are merely a presentation of information which is not a technical feature defining the product.
3. The subject matter of claims 1-19,24,25 and 28 are not anticipated by prior art documents D1-D5 and therefore fulfill the requirements of Art 33(2) PCT.
None of the prior art documents disclose a formoterol fumarate dihydrate (hereafter FFDH) having a water content of 4.8-4.28%wt.

Inventive Step

4. The prior art documents differ from the application only in that the formoterol fumarate dihydrate is not explicitly found to have a lower water content resulting from a drying step. The problem of stability regarding FFDH formulations is addressed in the prior art and is thought to be due to the presence of high concentrations of ethanol (cf. D3 and D4) and thus provides formulations with reduced levels of ethanol. D2 suggests the use of surfactants.

Thus the prior art provides several solutions to the problem.

The problem to be solved is seen as "how to provide an alternative stable aerosol formulations of formoterol fumarate"

The solution as provided by the applicant is the use of formoterol fumarate dihydrate having a water content of 4.8-4.28%wt.

D5 uses nedocromil salts to improve formoterol fumarate suspensions by reducing the moisture sensitivity of the active agent. However, it does not teach nor suggest reducing the water content of the active agent itself.

Therefore the application has provided an alternative way of stabilizing FFDH aerosol suspension.

However, the present application does not provide any evidence that the posed **problem has been solved** in the form of comparative stability data in order to show that this alternative provides a **special technical effect** over prior art. For instance D1 and D4 all provide formulations comprising the same components achieving the same effect, i.e. stability.

Therefore claims 1-19,24,25 and 28 in the absence of evidence that the problem has been solved, cannot be considered as involving an inventive step (Article 33(3) PCT).